# EXHIBIT R

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# The Breakdown of Polypropylene in the Human Eye: Is It Clinically Significant?

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*Polypropylene intracameral sutures and intraocular lens haptics have been reported to develop cracks after varying lengths of time within the eye. A study of the degradation of a 10-0 polypropylene suture and the absence of noticeable degradation on a 4-0 polypropylene intraocular lens haptic removed five years and three months after implantation is presented. The relationship of the molecular orientation of the polypropylene suture to the clinical significance of its cracks is discussed.*

Polypropylene is a semicrystalline thermoplastic that is used in the eye both as an intracameral suture and as an intraocular lens (IOL) haptic. Polypropylene (PP) sutures offer the advantages of flexibility, high tensile strength, and biological inertness. They have found increased use since the 1978 report by Drews[1] that documented by scanning electron microscopy (SEM) the complete disintegration of several intraocular nylon sutures. While both PP and nylon sutures are relatively nonreactive in both the chemical and physiologic sense, PP carries a lower risk of intracameral degradation.[2]

Before the popularization of polypropylene in ophthalmic surgery, its physical characteristics led to its enthusiastic use as a suture material in general surgery. Its use in intraocular surgery presents a special situation, however, as transmission of light through the cornea subjects the sutures and haptics associated with an intraocular lens to an additional degradative stress. Numerous investigators have studied the effect of ultraviolet (UV) light on polypropylene haptics and suture material to better define potential problems.

Lerman[3] exposed PP discs in vitro to near-UV light, (wavelengths of light between 300 and 400 nanometers), simulating the portion of the UV spectrum transmitted through the cornea. He concluded that physiologic exposure to ambient solar radiation would not degrade the polypropylene haptics used in IOLs. Lerman also reported similar unpublished results by E.T. Goldberg, who used PP sutures rather than discs. Work by Fechner[4] compared the effect of near-UV radiation on PP sutures to that on the polyethylenglycolterephthalate (PETP) sutures popular in West Germany. While he found that the PETP sutures were more resistant to UV radiation than the PP sutures, he concluded that "the part of the UV spectrum that reaches the iris is unlikely to degrade polypropylene sutures during the remaining life of an elderly patient who spends much time indoors."

Realizing the need for a reliable in vivo study on the degradation of PP sutures, Drews[5] studied the scanning electron micrographs of PP suture material removed from seven patients after intervals ranging from two months to five and one-half years. The micrographs showed a slow surface degeneration of the intraocular sutures of "questionable clinical significance." Recently, Apple and coauthors[6] presented SEM evidence of similar cracks seen in the PP haptics of three intraocular lenses removed after 15 to 45 months in the eye.

In our patient, a polypropylene iris fixation suture and a Binkhorst iris-clip 4-loop lens with PP haptics were removed five years and three months after implantation and studied by SEM. As is discussed below, surface cracking and flaking was observed on the suture and not on the haptic. This raises the important question of the degree of a cracked suture's susceptibility to fracture. From these findings, we discuss the relationship between the surface cracking seen in this suture and the changes in its mechanical properties as a result of this damage.

### Report of a Case

A 76-year-old Caucasian woman underwent extracapsular cataract lens extraction and intraocular lens implantation with an IOLAB Binkhorst iris-clip 4-loop lens in her left eye on June 15, 1978. A 10-0 polypropylene (Prolene-Ethicon) suture was loosely tied between the superior-anterior haptic and the superior portion of the iris to prevent a future dislocation of the IOL. Six months later, the patient required surgical repositioning of the IOL, which had dislocated and caused the inferior haptic to come forward and briefly touch the corneal endothelium.

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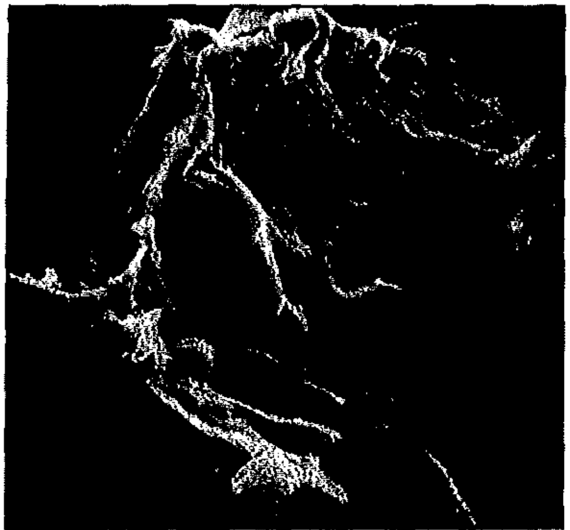


Figure 1. Inflammatory tissue adherent to 10-0 polypropylene knot (×220). The 10-0 polypropylene tails seen at the left and lower borders exhibit degradation (cracking and flaking).

On February 7, 1980, the patient's left eye had a corrected visual acuity of 20/200. One-plus cells were noted in the anterior chamber, and fine keratic precipitates were seen on the Binkhorst lens. Chronic cystoid macular edema was noted, and a diagnosis of chronic uveitis secondary to the intraocular lens was made. Despite therapy, the patient's clinical condition deteriorated, and she developed progressive corneal decompensation and stromal edema. On September 14, 1983, the fixation polypropylene suture was cut, and the IOL was removed. The suture, which had been noted to be intact and unchanged when viewed within the eye under the slit lamp, showed no gross evidence of damage at the time of its excision.

The removed 10-0 polypropylene suture and Binkhorst iris-clip 4-loop lens were subsequently studied by SEM to determine if any clinically significant degradation had occurred in the five years and three months the suture and IOL had spent in the eye.

## Methods and Results

After removal, the suture was air-dried at room temperature, then mounted on an aluminum scanning stub and gold-coated before examination. A Jeol-35 scanning microscope was used to examine the sample.

Scanning electron micrographs of the iris suture showed it to be encompassed by a large growth of fibrous tissue (Figure 1). Although the rest of the suture lacked this fibrous tissue growth, it did show extensive circumferential cracking and flaking of its superficial layers (Figure 2). The thickness of the surface flakes was estimated to be 0.2 to 0.3 microns, whereas the thickness of the cracks was estimated to be 0.5 to 0.6 microns. Other areas of the suture showed multiple layers of flaking and irregular caliber (Figure 3). A control 10-0 polypropylene suture put

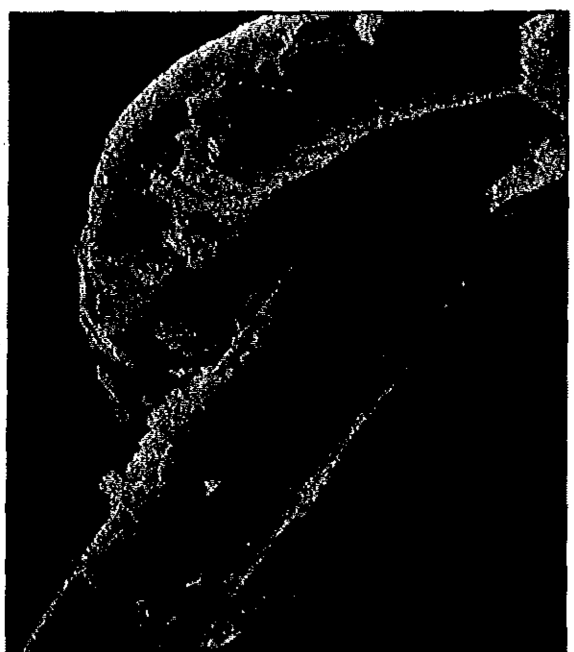


Figure 2. Circumferential cracking and flaking of the 10-0 polypropylene suture (×900).

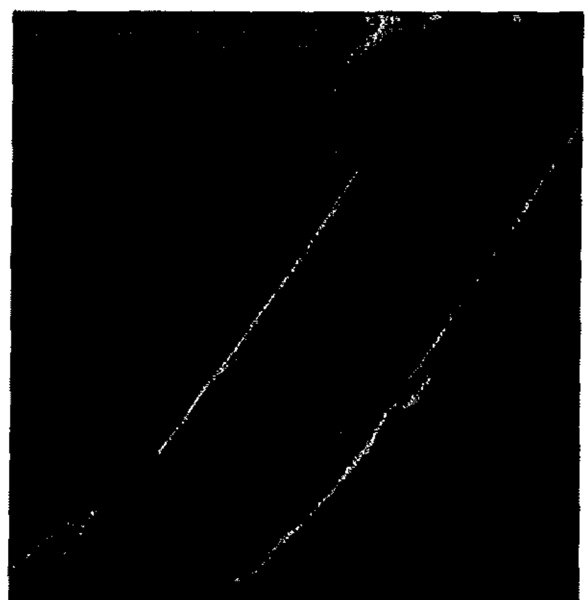
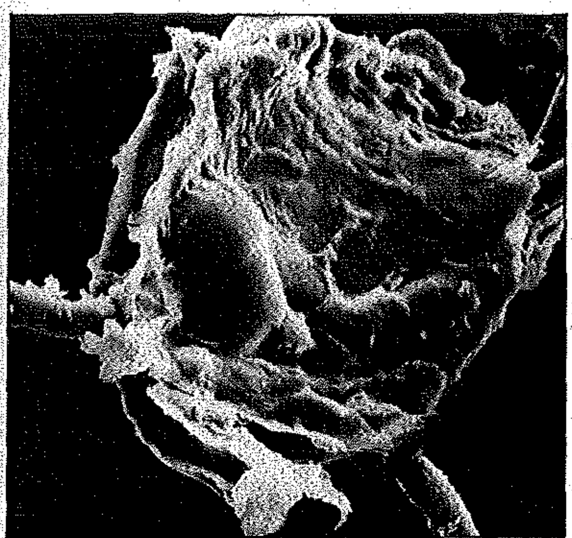


**Figure 3.** Degraded 10-0 polypropylene suture shows multiple layers of flaking and irregular caliber (×1000).



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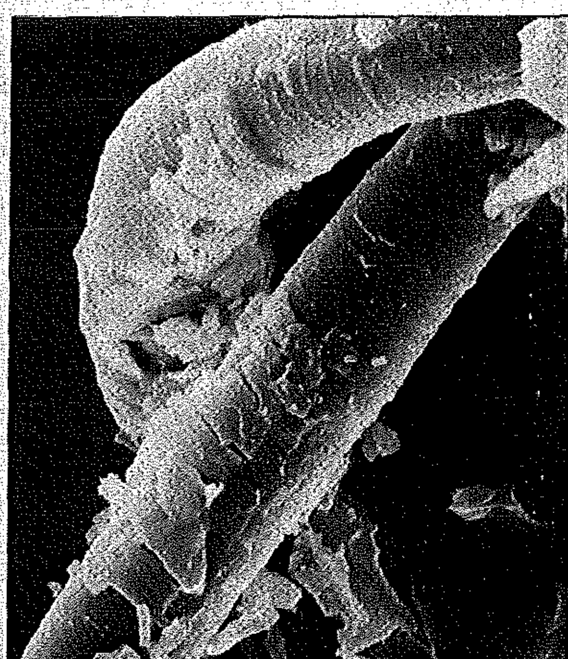
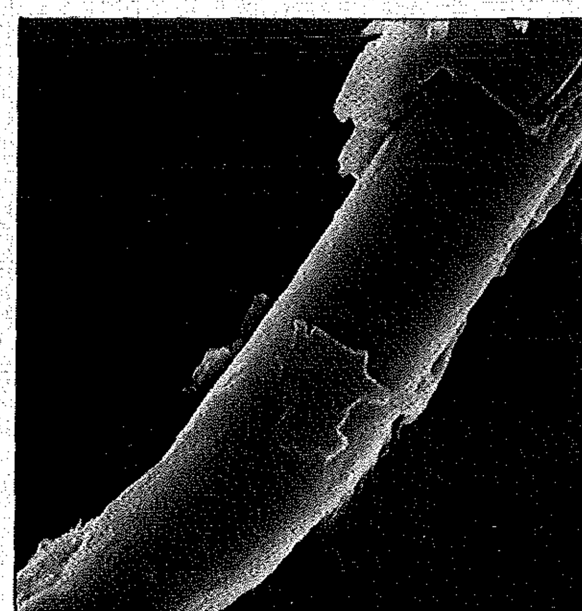


Figure 2. Circumferential cracking and flaking of the 10-0 polypropylene suture (×900).



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through the identical fixation process exhibited no cracks or flakes (Figure 4). Scanning electron micrographs of the polypropylene haptics of the iris-clip IOL also revealed no cracks or flakes (Figure 5). It did, however, reveal the normal longitudinal striations, which reflect the manufacturing process of polypropylene haptics.

## Discussion

The relatively thick 4-0 (200 microns in diameter) polypropylene haptic of the iris-clip lens did not exhibit any of the cracking or flaking that was seen on the fixation suture. This may be due to the suture, but not the haptic, passing through the vascularized iris stroma. Also, the manufacturing process that produced the suture may have been different from that which produced the haptic, resulting in a difference in breakdown susceptibility. (Note the difference in surface characteristics between the polypropylene suture and the haptic in Figure 4.)

Our interpretation of the morphology of the more fragile 10-0 suture (23 microns in diameter) is as follows. As shown in Figure 3 (×1000), when the outer "shell" of the polypropylene suture flakes off, we are left with an inner "core" of apparently undamaged PP. The existence of this undamaged core is a result of the oxidative forces on PP, and also reflects the manufacturing process of polypropylene sutures. Polypropylene is broken down by auto-oxidation of its molecular structure caused by polymeric radicals.[2] These radicals are formed by the absorption of ultraviolet light, heat, high-energy irradiation, mechanical stress, or the reaction of the polymer with radicals of a foreign source.[2] Additionally, these radicals form more readily in areas of the suture where small amounts of impurities exist.[7] In the thermal process resulting in the extrusion of the PP filament, photosensitizing microimpurities, (predominantly carbonyl and peroxide products), form on its exposed outer shell,[7] rendering it especially susceptible to peroxide radical formation, auto-oxidation, and the resultant cracking and flaking observed with SEM.

The cracks in the suture are limited in depth because the amount of impurities is negligible except on its outer surface, and hence the bulk of the filament remains unoxidized.[8] It is well known that this cracking weakens the suture, but the degree to which it does so is difficult to quantify. Garton[8] has shown that the "photo-oxidation–induced restructuring of the surface layer of PP monofilaments results in deep cracks that can propagate under stress, greatly embrittling the sample" and causing its true tensile strength to be significantly less than one would predict solely on the basis of the relatively minor decrease in cross-sectional

Figure 5. The 4-0 polypropylene haptic of Binkhorst lens, removed after five years (×330). A thin inflammatory membrane is seen over most of the haptic, yet no degradation of the polypropylene is seen. Fine longitudinal striations are seen, which reflect the manufacturing process of polypropylene haptics.

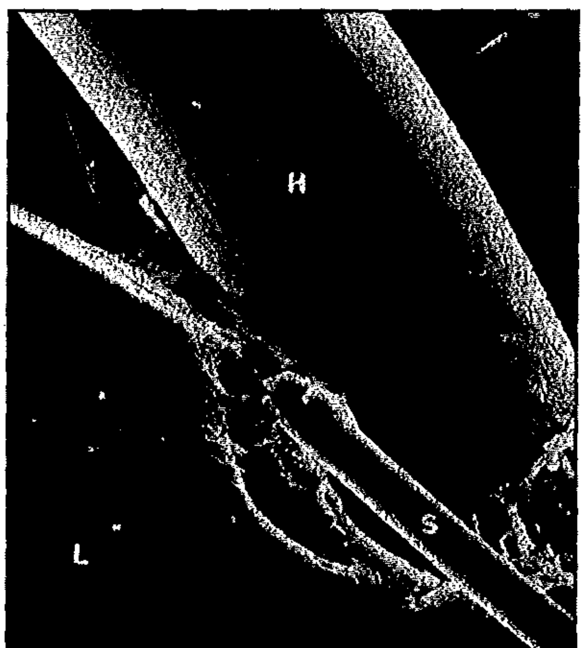


Figure 4. Control 10-0 polypropylene suture(S) (×300) from another case in which a McCannel suture was used intraoperatively to assist removal of a posterior chamber lens (L). (IOL removed after four months due to decentration.) Note the absence of polypropylene degradation in either the 10-0 suture(S) or the 4-0 haptic(H).

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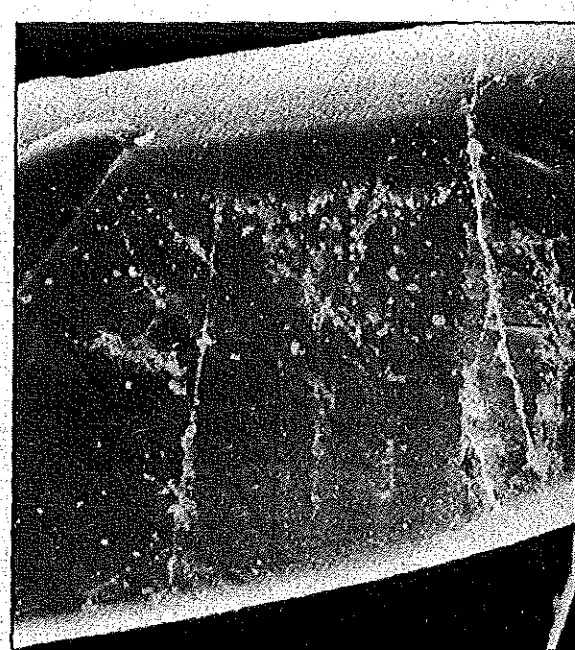

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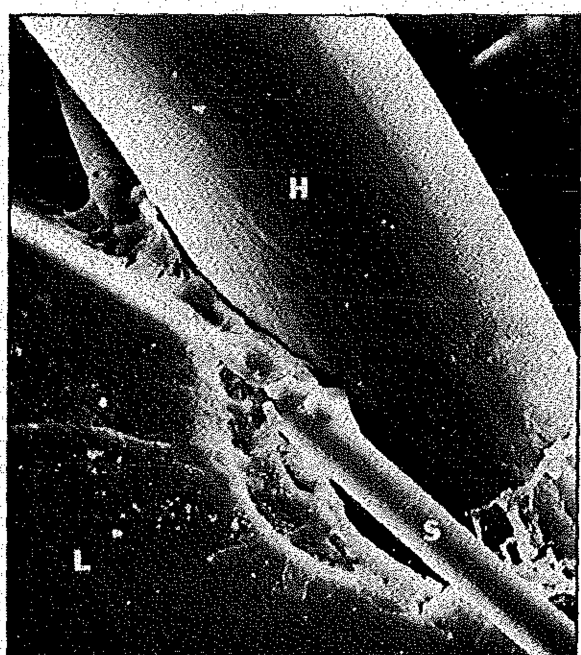



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diameter caused by the cracks. The extent of embrittlement (increased susceptibility to fracture) of PP was also shown to be dependent on the initial filament morphology, with the highly oriented fibers the least affected by UV irradiation, and the less oriented filaments progressively more susceptible to embrittlement. Other investigators have corroborated these findings, concluding that a cracked filament will behave like a notched rod, with subsequent mechanical stressing leading to "brittle failure."[9]

The degree of orientation that a monofilament can exhibit is determined by the degree to which it is "drawn," or stretched. Since drawing the fiber acts to align its constituent macromolecules, the more a fiber is drawn, the more highly oriented it will be. The maximum draw ratio that can be readily attained at room temperature for many polymers is on the order of six. This means that the suture can be stretched to six times its original length before breaking. Using special techniques involving varying temperature or solution spinning, the highest theoretical draw ratio attainable for commercial polypropylene is approximately 20 (Paul Smith, PhD, EI DuPont de Nemours & Company, Inc, Wilmington, Delaware, personal communication, 1984).

Independent analysis by Dr. Smith using wide-angle x-ray diffraction analysis showed that 10-0 polypropylene suture material "was drawn, after spinning, about three and one-half to four times, and that consequently, it was only a partially oriented fiber, and thus less resistant to chemical and physiochemical attack than a highly oriented fiber."

## Conclusion

All suture material implanted into the eye is subject to degradation, although the amount of degradation varies with the properties of the material in question, the sum of the degradative forces it is subjected to, and the length of time it is exposed to these forces. In procedures such as IOL implants, we must be fully aware of the ability of a suture material to withstand these degradative forces and appreciate the possible clinical consequences of late changes.

The examined 10-0 polypropylene suture was exposed to three separate sources of degradation for greater than five years: UV light, a chronically inflamed eye, and contact with the vascularized iris stroma. Although the suture did not break, areas of cracking and flaking were clearly in evidence. Because of the ensuing brittleness, the strength of the suture may have been compromised to a greater extent than the superficial cracking alone implies.

The polypropylene haptics studied in this case did not show degradation; however, recent studies of posterior chamber lenses with the haptics of this material have shown cracking and flaking in some cases.[9]

While the structural changes observed in the removed polypropylene material may have little, if any, clinical significance in the physiologic setting of an elderly person requiring an intraocular lens, further studies should be made before polypropylene comes into widespread use either as an intracameral suture or as an intraocular lens haptic in significantly younger patients.

The authors have no commercial or proprietary interest in Prolene-Ethicon nor any financial interest as consultants, reviewers, or evaluators.

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